Insulating Biomaterials N01-NS-2-2347

Thirteenth Quarterly Progress Report October-December, 2005

National Institutes of Health

National Institute of Neurological Disorders and Stroke

Neural Prosthesis Program

InnerSea Technology

1 DeAngelo Drive
Bedford, MA 01730

Contributors:

Dave Edell, PI

Robyn Edell, Testing

Sean Sexton, Instrumentation and Software

Ying-Ping Liu, Assembly and Testing

Karen Gleason, Chem Eng (MIT)

Shannan O'Shaughnessy, Grad Student, Chem Eng (MIT)

The goal of the Insulating Biomaterials work is to identify and evaluate materials, coatings, and assembly techniques suitable for protection of integrated circuit devices being considered for neural prosthetic applications.

Instrumentation Systems

Accelerated detection of degradation is the main tool for studying materials for implantable devices. The new Passivation Test System consists of 4 major components: the Tube Top, the Measurement Unit, the Data collection Unit, and the Calibration Unit. These components are described below. Basically, as illustrated in Figure 1 the device to be tested is placed into the saline soak tube.

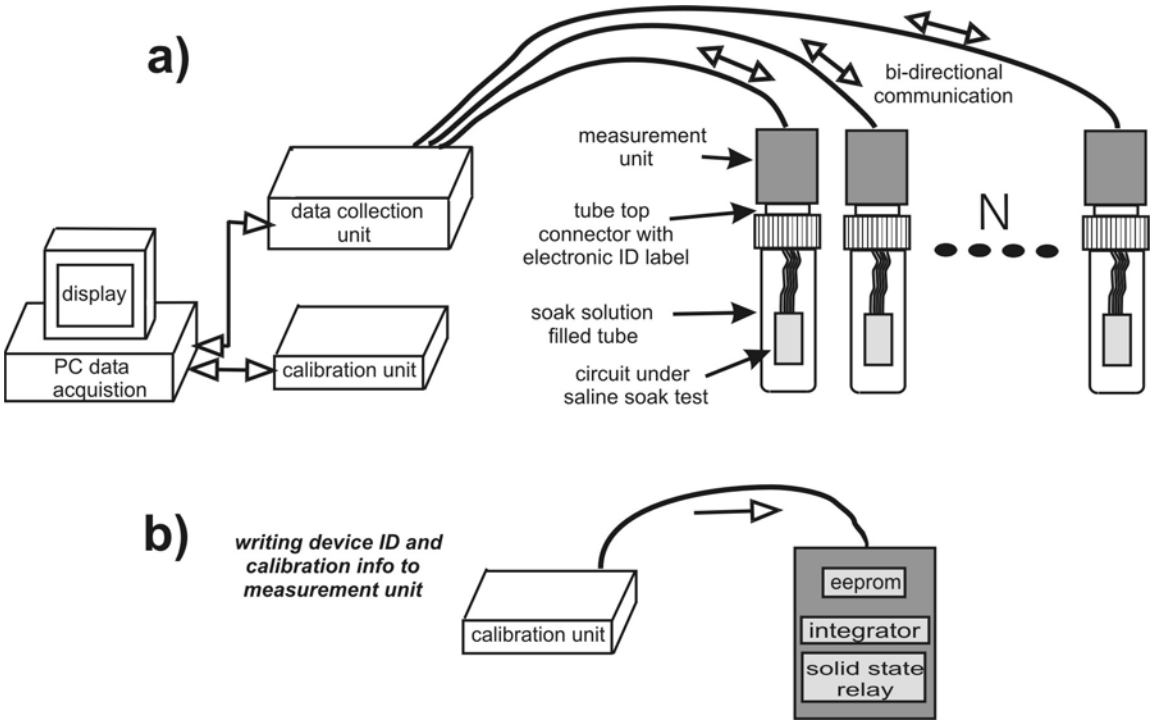


Figure 1: Cartoon showing basic elements of new test system.

1) the Tube Top - This provides: a physical attachment point for the device under test; the electrical connections to the system; and an EEPROM that contains information about the particular device in that is under soak test in that respective tube.

2) the Measurement Unit - This contains: the analog circuitry required to perform the measurement; a calibration check unit; a continuity tester for triple

track devices; and another EEPROM which contains required calibration information.

3) the Data Collection Unit - This accepts the data (consisting of timing signals) from the measurement units, converts them into leakage values, and transmits those values to a host computer.

4) the Calibration Unit - This is a standalone unit that is used with each device before any testing at all is performed, and it is normally used only at the onset of testing. Thus, if a device is tested each day for 100 days, the Calibration Unit is “hooked” up to Measurement Unit at the start of day 1 so that device identification data can be downloaded to the EEPROM that is located on the Tube Top, along with the calibration information particular to the device under test and that will be needed for the Measurement Unit to interpret the measured parameters for every succeeding test day.

Recent Results:

During this period, modifications were made to the new pass test system to prevent component failure during the connection and disconnection of devices. A small board called the Hot Swap Controller has been added to the instrumentation chain. This controller is designed to provide a “soft connection” when a measurement unit is added to a data collection unit. Once a unit is plugged in, the circuit ground is immediately connected, allowing any voltage transients present to dissipate safely through the transient suppression devices on the controller. After two seconds, the power supply is connected, followed by the digital control lines, the serial bus, and the analog signals. LED’s on the controller indicate a proper connection has occurred, and the data collection unit receives a signal that the measurement unit is now connected.

With the addition of this controller, the hardware chain is now complete. The data collection units and the hot swap controllers are ready for fabrication. Fabrication will be performed by Lightspeed Manufacturing of Methuen Massachusetts.

On the software side, development has begun using Visual Basic .NET; the newest development platform from Microsoft. .NET allows much greater flexibility, and communication options than our current development platform, Agilent VEE.

Peel testing for evaluation of adhesion:

New tests:

MED4860

Two samples were created for pull testing to determine the adhesive qualities of MED4860. MED4860 is a two-part platinum catalyzed liquid silicone rubber (LSR) developed for injection molding of chronically implantable devices. This material is of interest as a wire coating since currently available wire coatings will not bond with other platinum catalyzed elastomers. This material is also of interest because it is a currently FDA approved for chronic implantation. Samples were created following the usual procedure of adhering a microscope slide to an aluminum slide, adding strips of kapton tape and then adhering a length of large-weave, 12.5mm wide fiberglass tape to the glass slide using the silicone adhesive in question. At this point, the units were allowed to cure at room temperature overnight and then placed in a 150^{o} oven for 3 hours. After cooling, MED4-4220 was used to cover the unit to prevent corrosion of the aluminum substrate and it was returned to the 150^{o} oven for another 3 hours. The samples were created on 12/5/05 and the first, dry pull evidenced peak pull forces of 781 and 584 gms, well below forces evidenced with MED4-4220. Mechanical failure was at the interface.

MED4-4220 Lot 36069

This test was undertaken to determine whether the new lot of MED4-4220 behaved as previous batches of the silicone have. Two samples were created following normal procedures and incorporating kapton strips. The samples were created on 12/3/05 and the first, dry pull evidenced peak pull forces of 3266 and

3201 grams. These forces are characteristic of forces using previous batches of MED4-4220. Mechanical failure was due to the bulk material.

XL110 Cross-linker

Three samples were created using various concentrations of XL100, a crosslinker, with MED4-4220, LOT35070. The standard construction of the samples was employed, but the MED4-4220 that was used to adhere the fiberglass tape to the microscope slide had additional crosslinker (XL110) added at concentrations of .005, .01 and .02 times the weighted volume of MED4-4220 and then centrifuged to thoroughly mix. The samples were created 10/4/05 and three measurements have been taken. The .005 concentration has an average peak value of 3294 gms. (std. dev. 181), the .01 sample has an average peak of 2736 gms. (std. dev. 348) and the .02 sample has an average peak value of 2933 gms. (std. dev. 62). Failures were due to the bulk material. Early indications, then, are that there does not appear to be a connection between concentration of XL110 and increased adhesion during short term testing.

Samples with Observed Changes:

N-(2-Aminoethyl)-3-Aminopropyltriethoxysilane

N-(2-Aminoethyl)-3-Aminopropyltriethoxysilane is an organosilane coupling agent with a slower hydrolysis than other orgnosilanes. This sample has shown a marked decline in adhesion during the quarter, dropping from a high of almost 3000 gms in the previous quarter to a low of 1680 gms this quarter. Where the silicone had been left on the slide in the previous months, the slide surface where peeled is now without any silicone remaining indicating surface interfacial failure.

Allyltrimethoxysilane

Allyltrimethoxysilane is an organosilane adhesion promoter for vinyl-addition silicones. This test employed the allyltrimethoxysilane pretreatment on MED4-4220. The sample had been producing an adhesion in the 3000-3400 gm peak value range, but the last two pulls have diminished greatly and the last had fallen

to almost 2700 gms. Mechanical failure was both at the interface and in the bulk material as there were bare areas on the slide surface as well as residual silicone in other areas.

Bis(triethoxysilyl)ethylene

Another organosilane, Bis(triethoxysilyl)ethylene also has greater hydrolytic stability. This pretreatment was used with MED4-4220 and produced a pull force in the 3000 gm. peak value range until the last pull, where it fell drastically to just over 2000 grams. Through all pulls, the silicone was evidenced on tape and slide indicating both bulk and interfacial mechanical .

Butenyltrimethoxysilane

This pretreatment, used with MED4-4220, is an organosilane ester with hydrolytic stability. Pull force has steadily declined from an initial peak pull force of almost 3500 gms to the last pull of less than 1500 gms. The amount of silicone remaining on the slide has decreased as well indicating a weakening of the interface.

Final reports:

Vinyltriethoxysilane

Two samples were created using an aluminum slide base to which a cleaned glass slide was adhered.

A vinyltriethoxysilane solution was prepared using 95 ml. ethanol, 5 ml. distilled H_2O. This solution was adjusted to a pH between 4.5 and 5.5 using acetic acid. Two ml. of vinyltriethosxysilane was added after the solution was settled for 5 minutes. This solution was poured into a petri dish and the glass slide assembly was agitated in the dish for 1-2 minutes. One assembly was then dipped in another petri dish of ethanol, one in a dish of acetic acid and both placed on a teflon pad and baked for 5-10 minutes at 110^oC.

After cooling, the samples have strips of kapton tape added perpendicular to the slide and fiberglass tape added using MED4-4220.

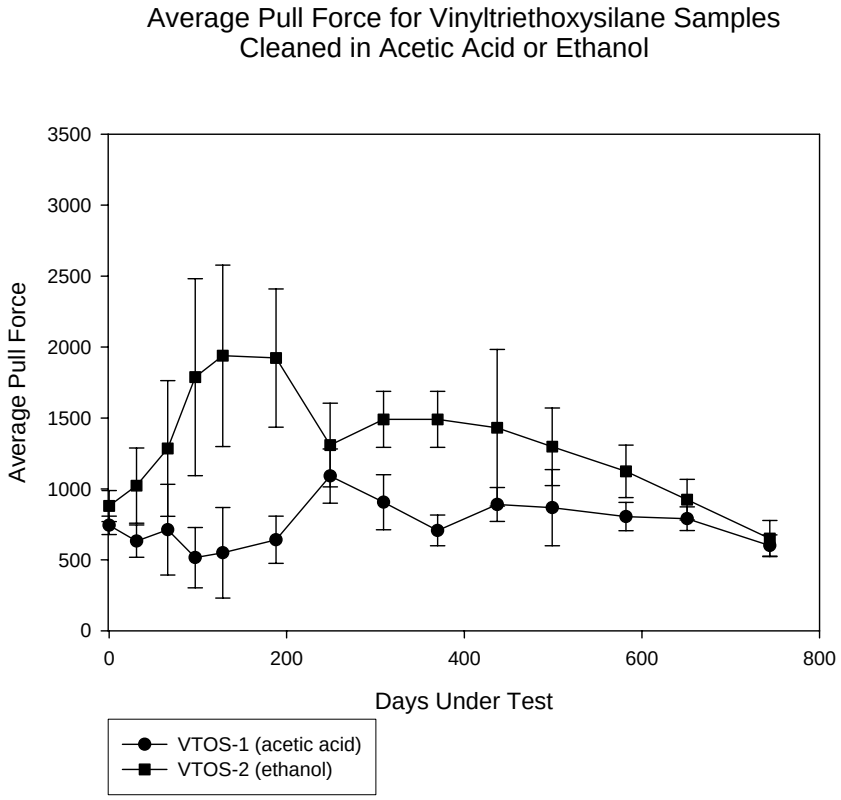
The assemblies were then baked at125^{o}C overnite.

The average pull force for the two samples were:

Rinsed in Acetic Acid = 748.69 gms.

Rinsed in ethanol = 1338.15 gms.

The ethanol rinsed slide had a much greater average pull force but at the conclusion of the pulls, the samples were very similar in pull strength and left silicone on the slide indicating bulk material failure which is odd for this material at these levels of peel force.



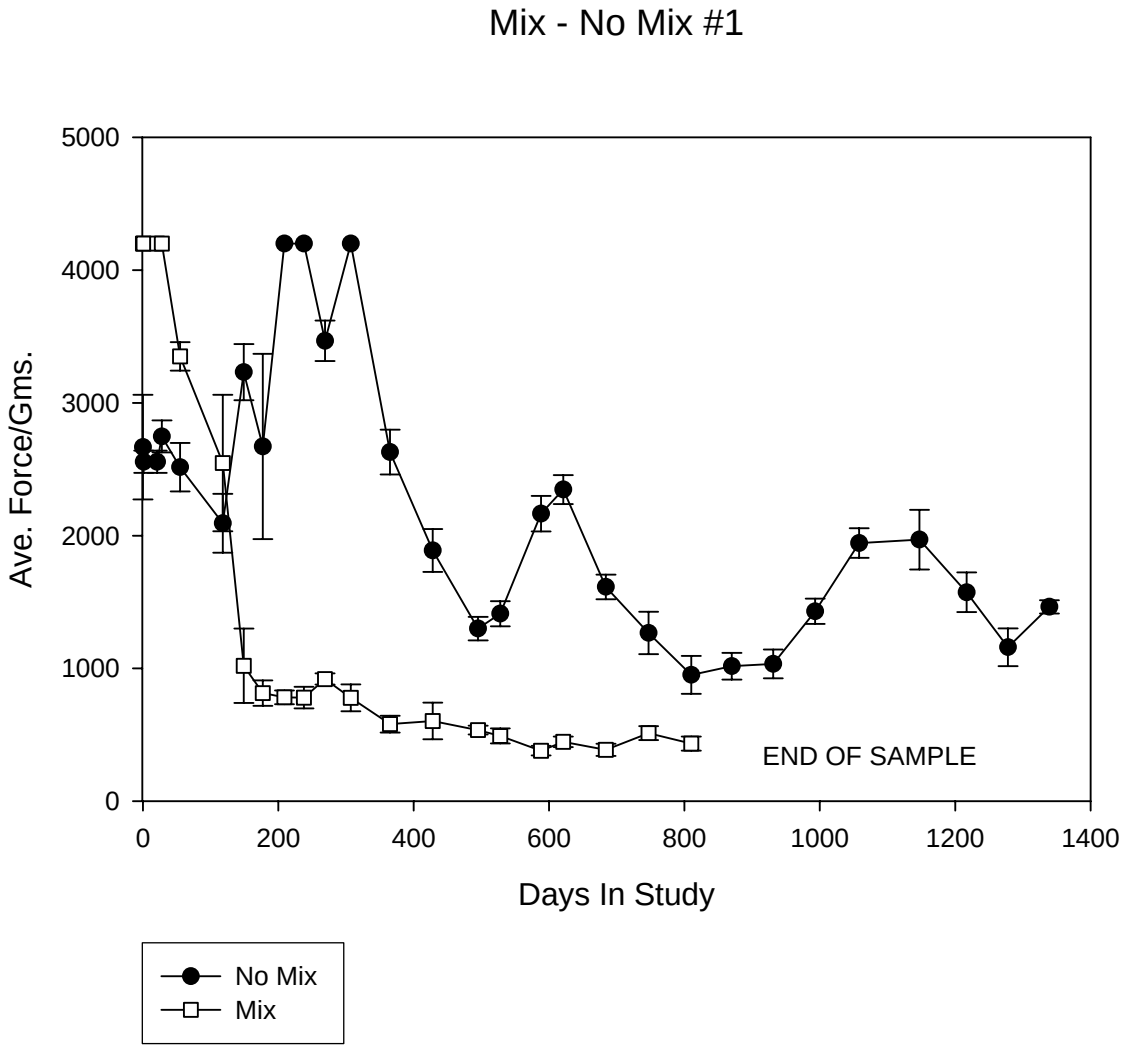
MED4-4220 Mix – No Mix

This study was undertaken to determine whether the mixing of the silicone affected its adhesion.

Two samples were created with microscope slides adhered to aluminum slides and lengths of .003 fiberglass tape adhered to these units with MED4-4220. One of the samples applied the silicone to the slide without mixing – directly from the

sxs kit. The other was adhered to the fiberglass tape after the silicone was mixed on the glass slide with a glass rod.

The sample that was not mixed had significantly greater pull force than the mixed sample. The mixed sample had an average pull force of about 1398 gms over the entire study of over three years. The sample that was not mixed had an average pull force over 3.5 years of 2146 gms. The mixing appeared to lessen the sample's adhesion qualities as there was no silicone residue left on the glass as there was in the sample not mixed.

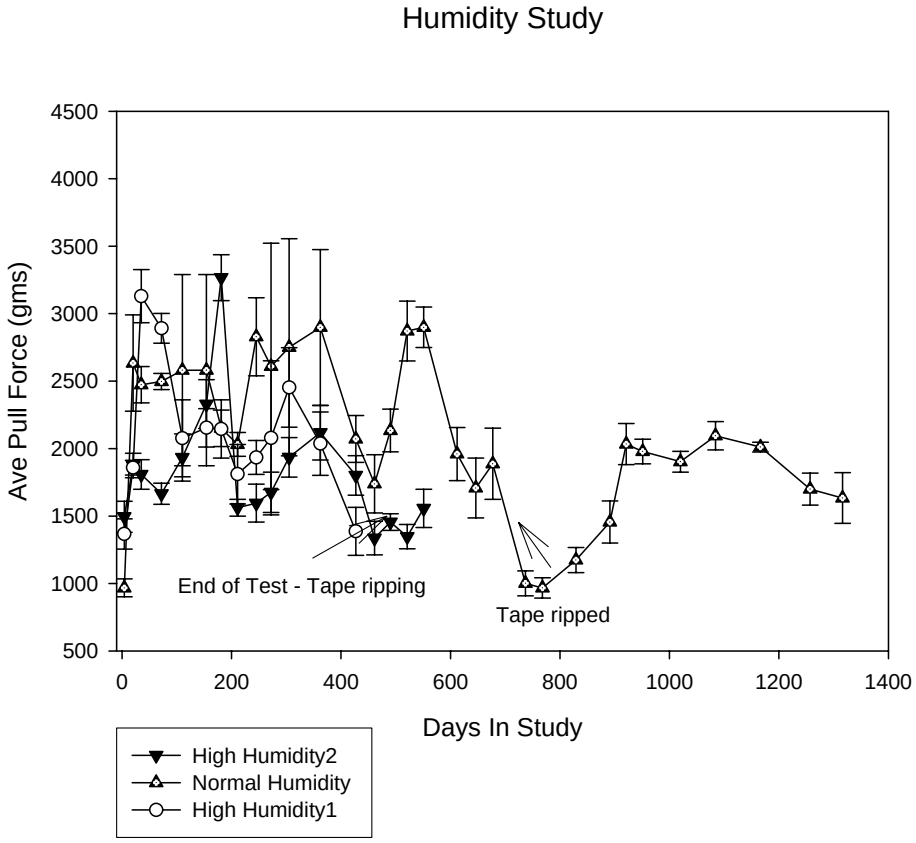


Humidity Study MED4-4220

Study to determine the effect on adhesion of changes in humidity during cure.

Two samples were created normally with a relative humidity in the oven of 1%.

Then two samples were created normally, but with an oven relative humidity of 39%. The humidity was raised by introducing a pan of distilled water into the oven prior to the curing of the samples.



Results:

The normal humidity sample labeled NORHUM2 was discontinued after 5 pulls as the tape was tearing. Results are not presented for that sample as it had such a short life.

The other normal humidity sample lasted for three and a half years. The high humidity samples lasted over a year and over a year and a half. Over the span of time the samples were all being tested, the high humidity samples pulled at a lower force than the normal humidity sample. Over the course of years after the high humidity samples were no longer tested, the pull force in the normal humidity sample dropped. Therefore, the average pull force for all samples

approached that of the high humidity samples. Mechanical failures were generally within the bulk material as there was silicone left on the slides after the pulls.

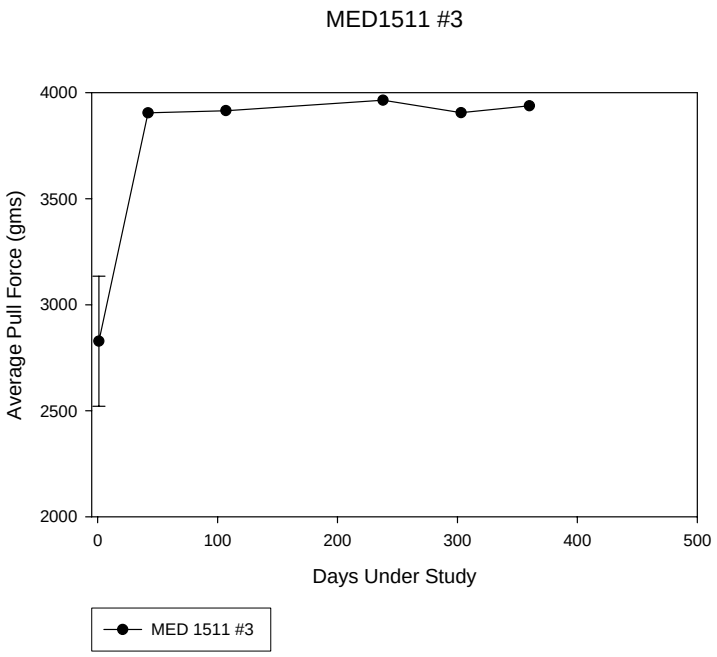
Discussion:

As the pull force measurements for the high humidity samples are lower than those seen for the normal humidity samples, it would seem that an elevated humidity level at cure may reduce the bulk mechanical properties of MED4-4220.

Final Report MED1511 #3

This sample was created using an aluminum slide base with quartz slide, cleaned with Vertrel, and IPA and DI in US cleaner. Kapton strips were applied across the quartz slide. MED1511 was applied to the slide assembly with a glass rod. Large weave fiberglass tape was laid along the slide unit and seated on the slide unit by using the ends of the tape to add pressure to make contact with the adhesive. The unit was allowed to air cure at room temperature.

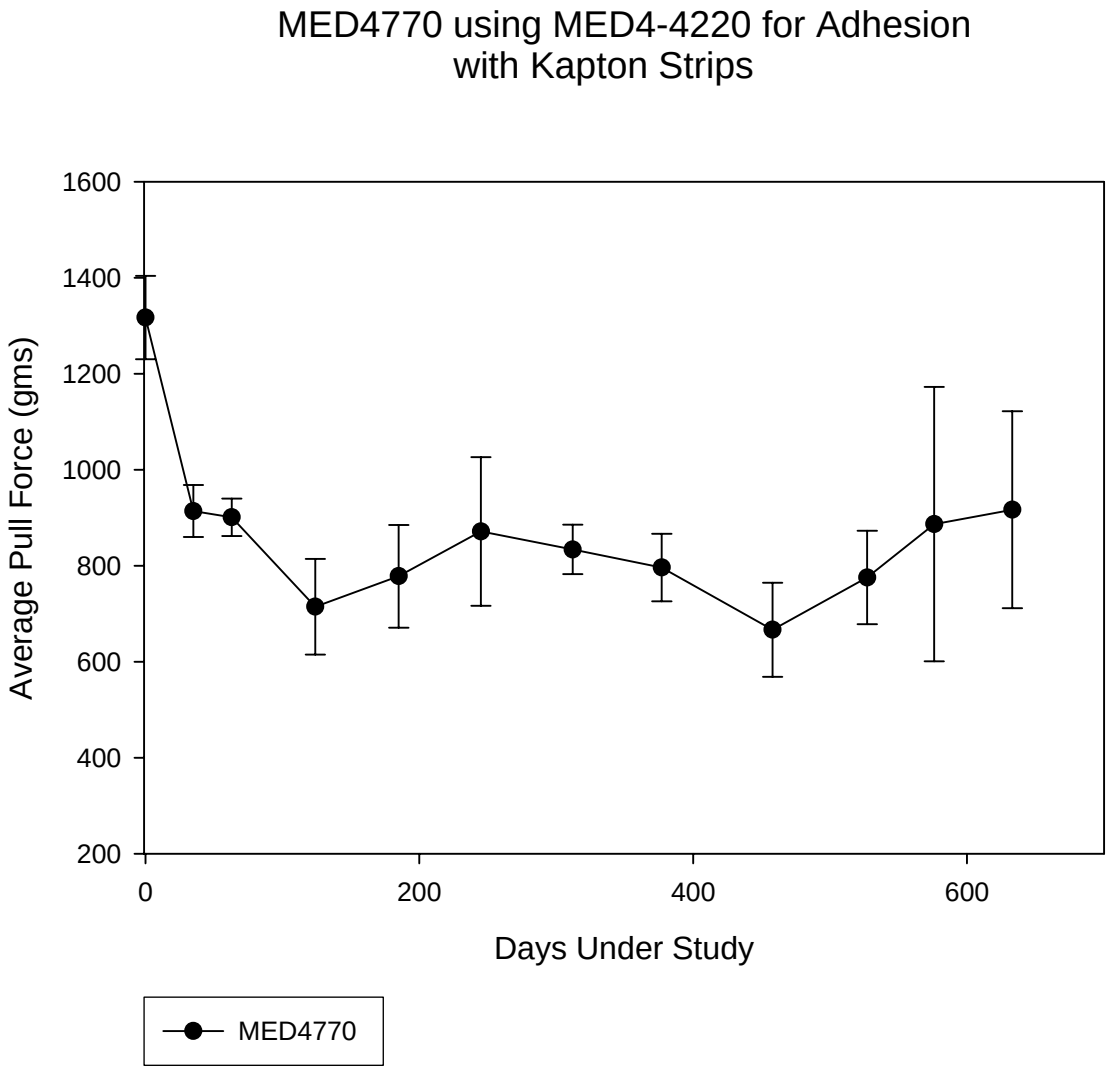
The sample maintained average pull force values above 3900 gms. after the initial dry pull. As with MED1511 #2, forces were excessive and failure was in the bulk material indicating extremely high adhesion for this material.



Final Report MED4770/MED4-4220

In this study, a pad of MED4770 was adhered directly to an aluminum slide using MED4-4220 and then baked at 125^{o} for 10 minutes. Strips of kapton tape were applied and then MED4-200 used to adhere the fiberglass tape. The unit was then baked for 3 hours at 125^{o}.

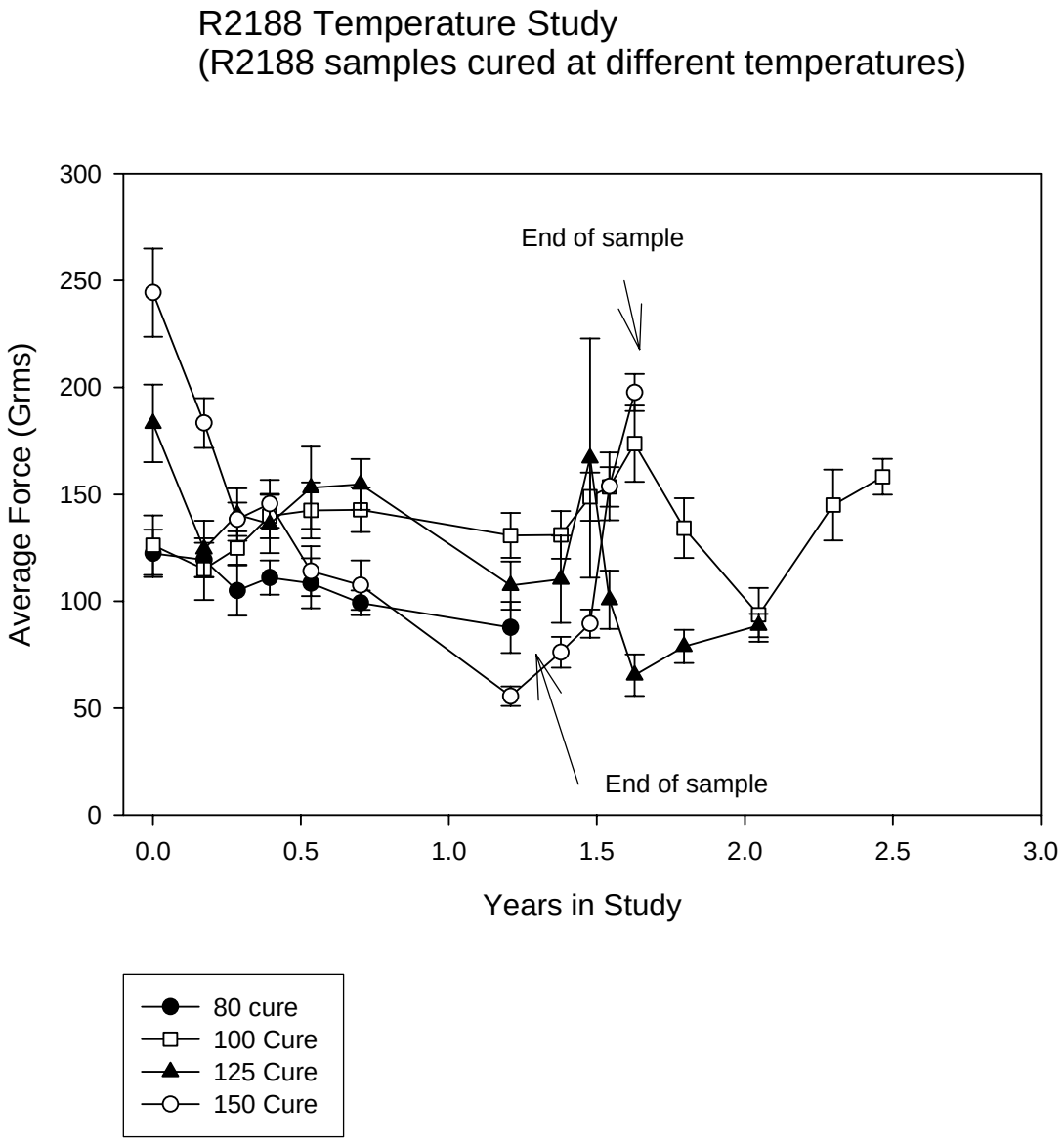
The pull test results averaged 868 gms. with a std. dev. of 165 gms.



Final Report Temperature Study R2188

Four samples were created with normal procedures for cleaning and adhering .007 fiberglass tape to slides. Each was cured at a different temperature: 80°, 100°, 125°, and 150°.

No clear difference appears from the samples, though the 80° sample was, for the most part, the worst performer in pull force.

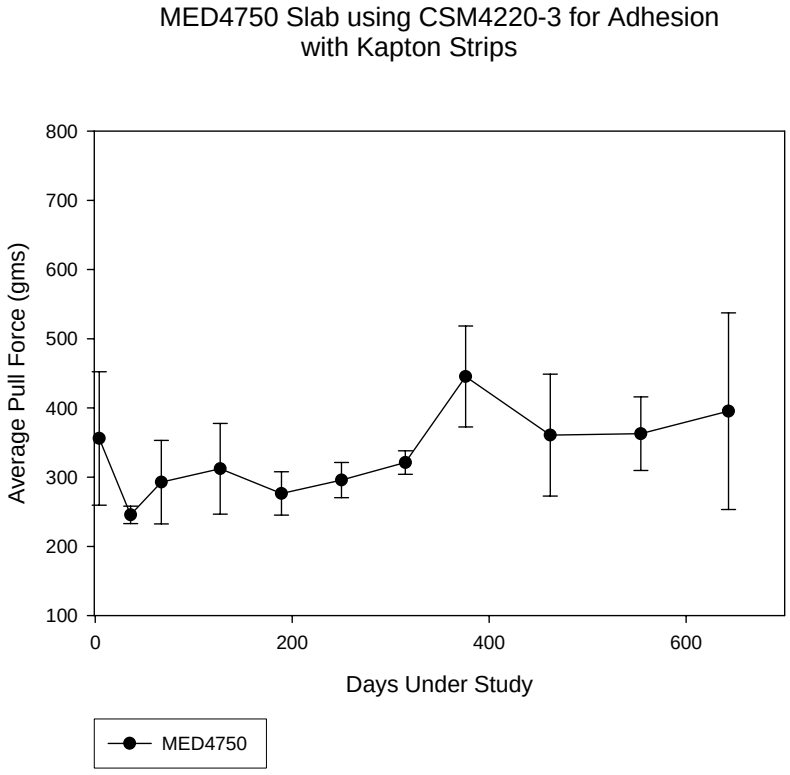


Bonding of Silicones to Silicones

This work was undertaken to identify a suitable extrudable material for coating interconnect wires such as wires from a subcutaneous battery or telemetry unit to an implanted device. As received wires from silicone extrusion manufacturers could not be reliably bonded to with any of the existing silicones available to us. If an extrudable silicone could be identified that has sufficient residual vinyl groups to bond reliably with proven encapsulation silicones, then a reliable assembly can be accomplished.

MED4750 – CSM4220-3

This study was undertaken to determine the adhesion of CSM4220-3 to a slab of MED4750. The slab of MED4750 was adhered to an aluminum slide and then .007 fiberglass tape was adhered to the slab using CSM4220-3. The results were typical of CSM4220-3 on glass slides – roughly 250-300gms. pull force on average. The tests were halted as no variation was seen in this sample as with most CSM4220-3 studies.

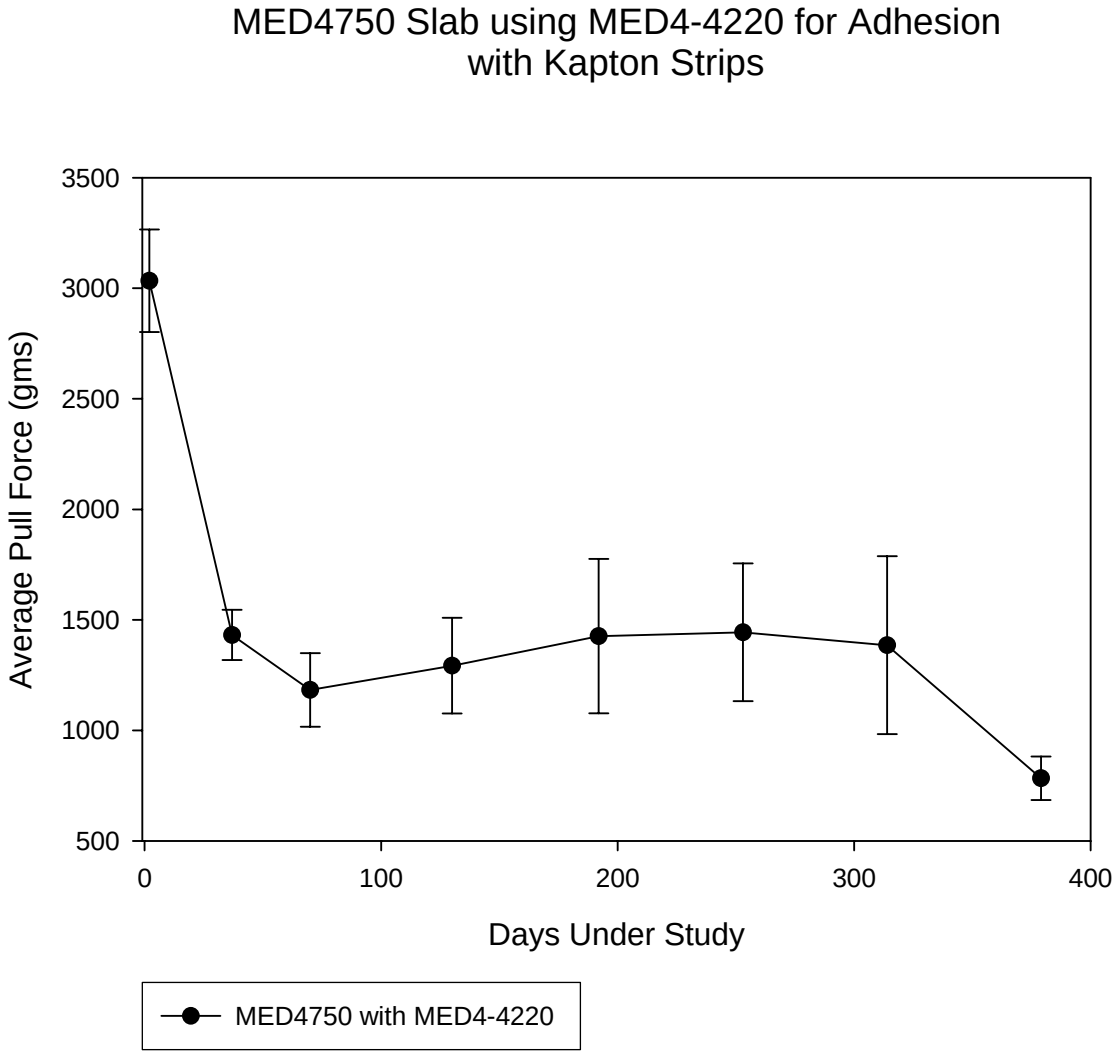


MED4750/MED4-4220

This study was undertaken to determine the adhesion of a slab of MED4750 with MED4-4220.

Sample was created by cutting a slab of MED4750 the size of aluminum slide (1"x3") and cleaning slab and slide. The two were adhered using MED4-4220 and baking. Kapton strips were applied and MED4-4220 spread on the sample and .007 fiberglass tape adhered. Sample was then baked.

Results show an average pull force over all tests to be 1505.83 grams.



Uptake ATP/Albumin

Over the course of this study of the effects on MED4-4220 and R-2188 immersed in ATP or albumin, the weight of the silicone disks has diminished. In this quarter, the weight change has been very marked. All 4 samples are now below initial weight by almost .2% to almost .5% normalized.

Uptake NaCl

As with the ATP/Albumin study, the uptake of the silicones in NaCl has produced a steady decline in weight of the disks. The MED4-4220 disk has declined by almost .15 % and the R-2188 disk has declined by almost .25 % normalized.

Mechanical Samples

RPT4, implanted and soaked PT4220 silicone spaghetti samples

Five groups of silicone spaghetti samples were created using MED4-4220 to determine the long term mechanical (and chemical) stability of this encapsulant.

RPT4A was implanted in a rabbit 6/5/00. Samples were harvested 6/26/00 when the animal stopped eating. Results of pull tests show a universal decline in elasticity (Young's modulus calculations). Average initial pulls prior to implantation were about 8550 gm/cm^2. Average pulls after removals were about 8000 gm/cm^2.

RPT4B was implanted 6/8/00. Samples were harvested and pulled 11/10/05, after approximately 2000 days. These samples showed an increase in elasticity using Young's Modulus. Initial pulls showed an elasticity of approximately 8500 gm/cm^2 on average. After removal, the samples showed an average Young's Modulus value of about 10000 gm/cm^2.

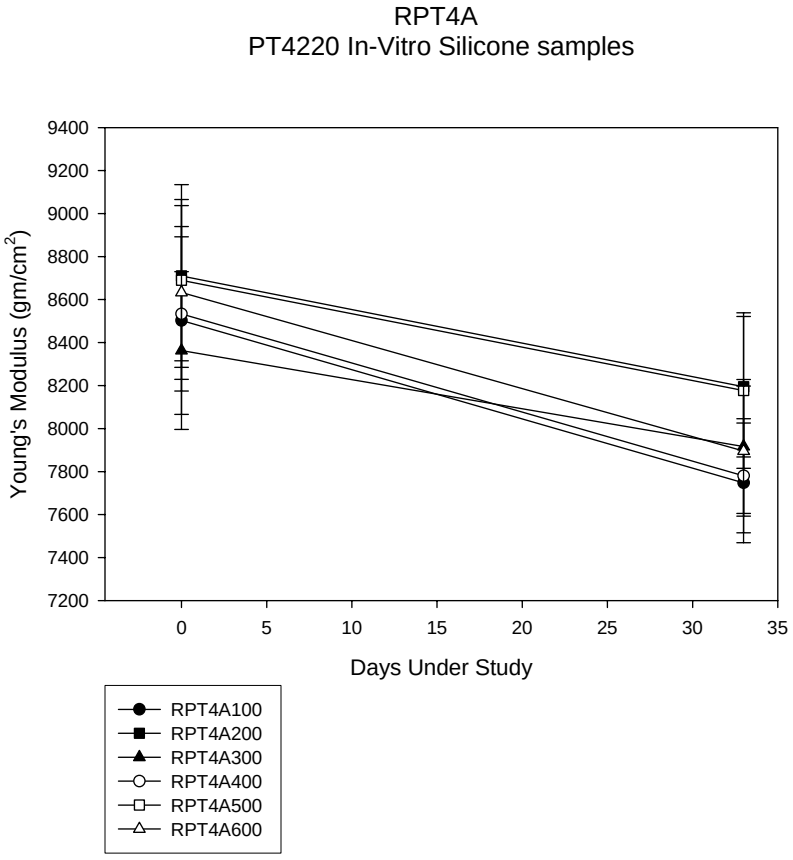
RPT4C samples were temperature treated and placed in air or H_2O. The sample heated to 90^0 and placed in H_2O began at approximately 8500 gm/cm^2 and has risen to approximately 11750 over 2000 days. The sample heated to 80^0 and placed in H_2O began with values around 8750 gm/cm^2 and has risen to approximately11750 gm/cm^2. The sample unheated and placed in an air

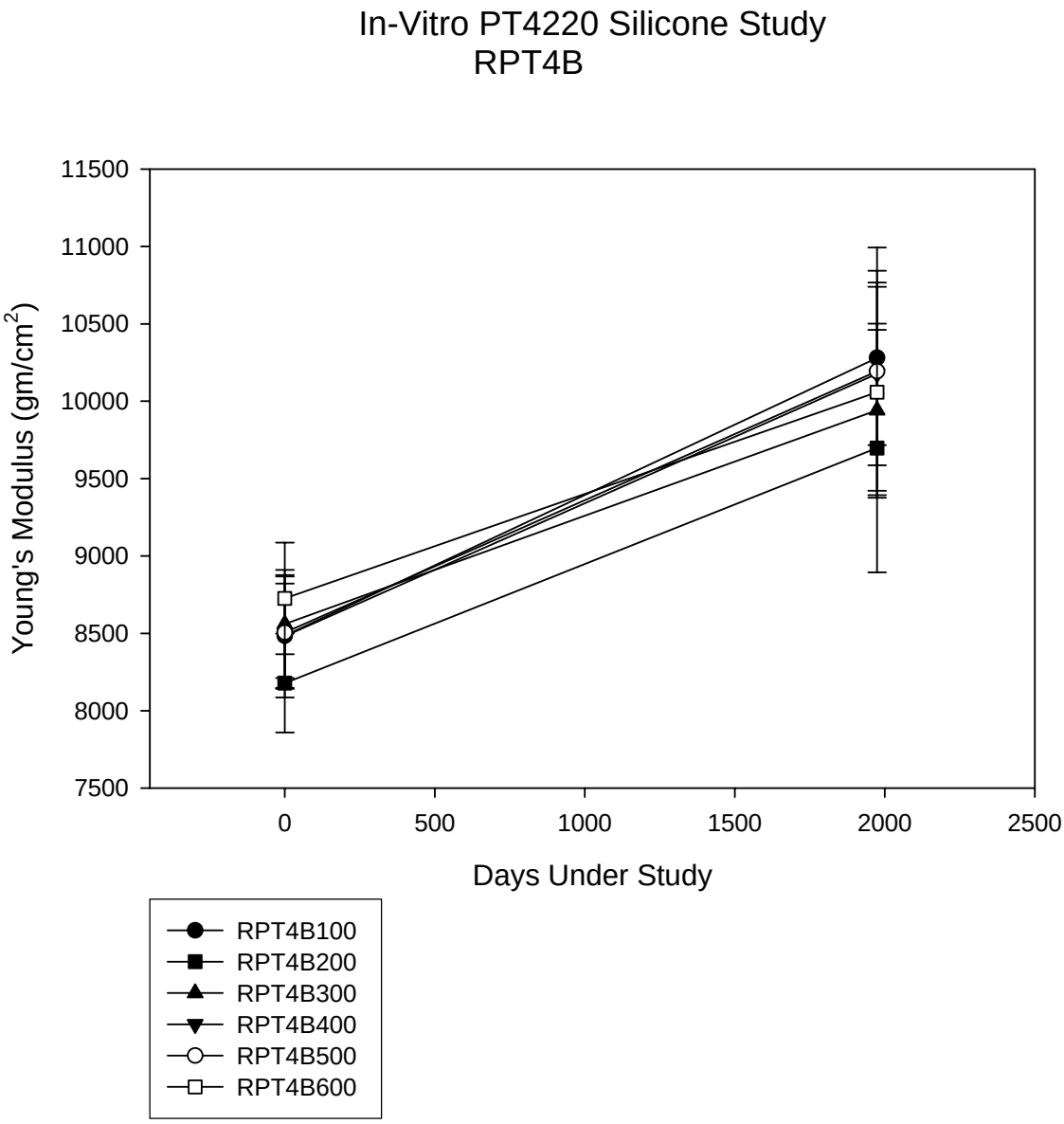
environment started at approximately 850 gm/cm^2, dipped initially to just below 8000 gm/cm^2 and has risen to approximately 9750 gm/cm^2.

RPT4D samples were too fragile and were not implanted.

RPT4E samples were created and implanted 3/23/01. Two samples were removed at one year and showed a decline in elasticity. Original measurements were at about 11600 gm/cm^2. They declined to between 10300 and 11100 gm/cm^2. After 2 years, two more samples were removed. One began with a value of approximately 11650 gm/cm^2 and remained at that value after 2 years. With the other sample, an original value was not found due to a lab error, so it was not possible to relate the subsequent value of 10900 gm/cm^2. Two more samples are available for removal at the five year mark in 3/06.

These results indicate thus far that MED4-42200 is relatively mechanically (and thus chemically by inference) stable during long term implantation.




In-Vitro PT4220 Silicone Study
RPT4B
Young's Modulus (gm/cm2)
11500
11000
10500
10000
9500
9000
8500
8000
7500
0
500
1000
1500
2000
2500
Days Under Study
RPT4B100
RPT4B200
RPT4B300
RPT4B400
RPT4B500
RPT4B600

CVD Deposition of Silicones

Work over the past months has focused on three areas:

1. Testing and optimization of coating surface roughness
2. Testing of coating dielectric constant, adhesion, and thermal stability
3. Composition of a journal article covering coating synthesis and reaction mechanism

1. Atomic Force Microscopy was utilized to examine coating roughness of films deposited under various conditions. A baseline root mean square roughness of 6.7Å was found for coatings deposited at the conditions utilized for the long term soak samples. In addition, it was found that this roughness could be optimized through the use of slightly lower filament temperatures (350°C vs. 500°C) a value of 3.7Å. This value is only slightly higher than that of bare silicon (which has an RMS roughness of 1.5Å) and should be suitable for all possible applications of the material.
2. Previous work had been performed to preliminarily asses the coating adhesion to a silicon substrate. Recently, further analysis has been performed to try and quantify this property of the material. ASTM tape test D3359-02 was utilized on film samples deposited on bare silicon wafer. The films showed a classification of 5B, which corresponds to the highest possible adhesion rating. In addition, this level of adhesion was not observed to change when the test was repeated on the sample after boiling in de-ionized water for 30minutes (a well established method for driving film delamination). Additional testing of film dielectric properties was also performed, with multiple samples showing dielectric constants between 2.4 – 2.8. It is not believed that further optimization in this area is required. Thermal stability of the films was also assessed for use integrating the film into a future probe manufacturing process. The film was seen to be stable to a temperature of 350C for a period of 30 minutes.

Further work will be done to move this stability level up to 400°C, which is the maximum requirement for any semiconductor process.

3. Composition of a journal article describing the novel polymer which composes the deposited films is underway. The article will focus on the synthesis and reaction mechanism of the material. There will also be a discussion of the reaction kinetics and the impact of utilizing an azo based initiator vs. a peroxide based initiator. A future paper will discuss material properties and film application. It is anticipated that the current manuscript will be submitted for publication in February 2006.